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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

WARNING LETTER

VIA FEDERAL EXPRESS

Mr. Marcel Burkart
President/Managing Director
Ortek AG
Industrie – Nord S
5634 Merenschwand
Switzerland

Dear Mr. Burkart:

During an inspection of your firm located in Merenschwand, Switzerland on April 13 through 15, 2004, our investigator determined that your firm manufactures shoulder, hip, and knee prostheses as well as orthopedic manual surgical instruments. These products are devices within the meaning of section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 321(h)).

This inspection revealed that these devices appear to be **adulterated** within the meaning of section 501(h) of the Act (21 U.S.C. § 351(h)), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. Significant violations include, but are not limited to, the following:

1. Failure to validate with a high degree of assurance according to established procedures a process for which the results cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a). For example:

   a. The sterilization process was not adequately validated for the following reasons:

      1) The methods used to perform to validate the [redacted] sterilization process are inadequate because they do not validate your sterilization process to a high degree of assurance. For example, there was no established protocol or method for performing the sterilization validation as required by the method referenced in your procedure. In addition, the testing performed includes only [redacted] which is insufficient for a complete sterilization validation. Your procedure states that validation of the [redacted] sterilization process will be performed based on an established standard referenced in your

procedure. However, the methods your firm used do not follow that sterilization validation reference standard.

2) Your sterilization assurance level (SAL) of [redacted] is only based on sterility testing of [redacted] product samples. The use of [redacted] product samples to establish the SAL is inadequate and does not follow your established sterilization validation procedure.

3) The devices have not been evaluated after [redacted] to determine that the devices are not adversely affected by the dosage; the current maximum dose specification of [redacted]

b. The packaging sealing process was not adequately validated for the following reasons:

1) The Installation Qualification was not documented;
2) [redacted] were used during the validation study, which does not represent actual conditions of use;
3) The validation study did not include evaluation of critical parameters such as temperature, time, and pressure; and
4) The validation test included only [redacted] of product without any statistical rationale.

2. Failure to establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met, as required by 21 CFR 820.75(b). For example:

a. You have not performed [redacted] dose audits, as required by your sterilization procedure.
b. The packaging sealing process for sterile barrier packaging is not monitored.

3. Failure to validate computer software for its intended use for computers or automated data processing systems used as part of production or the quality system, as required by 21 CFR 820.70(i). For example, the software used to control the automated [redacted] used to produce medical devices has not been validated.

4. Failure to establish and maintain adequate procedures for implementing corrective and preventive action, as required by 21 CFR 820.100. For example:

a. Your corrective and preventive action (CAPA) procedures do not include requirements for analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of

nonconforming product, or other quality problems. The CAPA procedures also do not include the methods for such analyses.

b. Your CAPA procedures do not identify when you will verify versus validate corrective and preventive actions to ensure that such action is effective and does not adversely affect the finished device.

c. There is no documentation that relevant information on identified quality problems as well as corrective and preventive actions is reviewed by management.

5. Failure to establish and maintain procedures for finished device acceptance that ensure that finished devices are not released for distribution until: (1) the activities required in the DMR are completed; (2) the associated data is reviewed; (3) the release is authorized by the signature of a designated individual(s); and (4) the authorization is dated, as required by 21 CFR 820.80(d). For example, the release of medical devices is not authorized by the signature of a designated individual nor dated, and there are no procedures for authorization to release medical devices.

6. Failure to establish and maintain adequate procedures for acceptance of incoming product to include the inspection, testing, or other verification that the incoming product conforms to specified requirements, as required by 21 CFR 820.80(b). For example, you do not review quality testing records for incoming raw materials and components to ensure that the results of the tests meet established specifications. In addition, it appears that acceptance or rejection is not documented.

7. Failure to establish and maintain adequate procedures to ensure that sampling plans are adequate for their intended use and reviewed when changes occur, as required by 21 CFR 820.250(b). For example, your sampling plan to sample every [redacted] and [redacted] device for in-process and finished device acceptance activities is not based on a valid scientific or statistical rationale.

8. Failure to establish and maintain adequate procedures for quality audits that require that quality audits be conducted by individuals who do not have direct responsibility for the matters being audited, as required by 21 CFR 820.22. For example, the [redacted] performs the internal audits of areas of the quality system that are under his direct responsibility.

9. Failure of management with executive responsibility to review the suitability and effectiveness of the quality system at defined intervals and with sufficient frequency according to established procedures to ensure that the quality system satisfies the requirements of 21 CFR Part 820 and the manufacturer's established quality policy objectives, as required by 21 CFR 820.20(c). For example, management review meetings are not conducted and documented and the [redacted]

procedure, [redacted] does not address the documents and activities that are to be submitted for management review.

10. Failure of management with executive responsibility to appoint, and document the appointment of, a member of management who has established authority over and responsibility for: 1) ensuring that quality system requirements are established and maintained, and 2) reporting on the performance of the quality system to management with executive responsibility for review, as required by 21 CFR 820.20(b)(3).

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, Form FDA 483 (FDA 483), issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and to bring your products into compliance.

Given the serious nature of these violations of the Act, the various orthopedic implant and surgical instrument devices manufactured by your firm and imported or offered for import are subject to refusal of admission under section 801(a) of the Act, 21 U.S.C. § 381(a), in that they appear to be adulterated. As a result, FDA may take steps to refuse these products including placing them on "detention without physical examination," until these violations are corrected.

In order to remove the devices from detention, you should provide a written response to this Warning Letter as described below and correct the violations described in this letter. We will notify you if your response is adequate, and we may need to re-inspect your facility to verify that the appropriate corrections have been made. In addition, U.S. federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of government contracts.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter, of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include all documentation of the corrective action you have taken. If you plan to make any corrections in the future, include those plans with your response to this letter as well. If the documentation is not in English, please provide a translation to facilitate our review.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement B, Orthopedic, Physical Medicine, and Anesthesiology Devices Branch, 2098 Gaither Road, Rockville, Maryland 20850 USA, to the attention of Pamela D. Scott.

If you need help in understanding the contents of this letter, please contact Pamela D. Scott at the above address or at (240) 276-0267 or FAX (240) 276-0129.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

Cc: Argomedical AG
Gewerbestrasse 5
Cham, Switzerland
CH-6330